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Heterosexual and Homosexual Patients with the Acquired Immunodeficiency Syndrome

A Comparison of Surveillance, Interview, and Laboratory Data

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Homosexual and heterosexual patients with the acquired immunodeficiency syndrome were compared by risk group. Race; diagnoses; history of sexually transmitted diseases, sexual behavior, and drug use; and socioeconomic indicators differed considerably among the risk groups, suggesting different risk factors for acquisition of the syndrome. Patients in the homosexual, intravenous drug user, and Haitian risk groups differed in their serologic response to cytomegalovirus and syphilis testing, presumably due to lifestyle-related exposures. Differences in the rate of recovery of cytomegalovirus, serum levels of IgA and IgG, and antibody titers to Epstein-Barr virus were noted among patients with different diagnoses. We conclude that in studies of risk factors for the acquired immunodeficiency syndrome, patients should be analyzed by risk group and diagnoses.

MOST PATIENTS with the acquired immunodeficiency syndrome reported to the Centers for Disease Control (CDC) in the years 1978 to 1982 were homosexual men. Therefore, the CDC undertook a nationwide case-control study of these men to identify risk factors for the syndrome. In the report of the epidemiologic results of this study, Jaffe and colleagues (1) noted an association between the syndrome and a certain homosexual lifestyle, in which the strongest correlate with disease was sexual contact with a large number of anonymous partners. However, no one behavioral factor was implicated as causal. A similar study has not been done to identify behavioral risk factors for heterosexual patients. Through a national surveillance system, the CDC has identified

the following subgroups of heterosexuals as being at risk for the acquired immunodeficiency syndrome: intravenous drug users (2-4), Haitian natives living in the United States (5), and patients with hemophilia (6). Although less firmly established as risk factors, being the sexual partner of an intravenous drug user or the recipient of whole blood or blood products may also increase the risk for acquiring the syndrome (7, 8).

Accumulating epidemiologic evidence indicates that an infectious agent is, at least in part, the cause of the acquired immunodeficiency syndrome. The agent is probably transmitted both sexually and through intravenous infusion of contaminated blood or blood products (8). Rogers and coworkers (9) have examined the laboratory data from the national case-control study of homosexual patients with the acquired immunodeficiency syndrome (cases). Although the authors found several serologic differences between "cases" and controls, the data did not point to a particular infectious agent as causal.

We have analyzed the similarities and differences between homosexual and heterosexual patients with the acquired immunodeficiency syndrome in demographic and behavioral characteristics and serologic evidence for infection with various organisms. We have attempted to define the links between the identified risk groups that make these groups susceptible to the same syndrome, and to differentiate between exposures characteristic of certain lifestyles and exposures common to all risk groups.

Methods

Our case definition included all persons older than 15 years of age reported to the Centers for Disease Control (CDC) as having Kaposi's sarcoma, *Pneumocystis carinii* pneumonia, or

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Table 1. Reported Cases of Patients with the Acquired Immunodeficiency Syndrome in the United States Compared by Risk Group, Race, and Diagnosis*

	Heterosexual Men and Women				Total Homosexual or Bisexual Men (n = 300)
	Drug User (n = 39)	Haitian (n = 16)	No Identified Risk (n = 9)	Total (n = 64)	
	← % →				
Race/ethnic group					
White	26	...	33	20	73
Black, not Haitian	44	...	23	30	17
Hispanic	28	...	33	22	10
Haitian	2	100	0	26	0
Other	0	...	11	2	0
Diagnosis					
Kaposi's sarcoma	3	6	44	9	34†
Pneumocystis pneumonia	77‡	50	56	67	44
Both diseases	3	0	0	2	16
Other infection	17	44§	0	22	6

* Cases reported as of 1 June 1982. Twelve men with unknown sexual orientation and one man with hemophilia are not included.

† $p < 0.05$, compared with drug users or Haitians.

‡ $p < 0.05$, compared with homosexual or bisexual men.

§ $p < 0.05$, compared with other risk categories.

other serious opportunistic infections; who had no underlying or immunosuppressive disease; and who had not received immunosuppressive therapy. Patients more than 60 years old with Kaposi's sarcoma were excluded because of the higher background prevalence of this illness among elderly men.

We used three different sets of data for analysis: data from surveillance reports sent to the CDC (10), data from a heterosexual interview study, and laboratory data from specimens tested by the CDC. Surveillance reports sent to the CDC (10) included the age, race, residence, sex, sexual orientation, history of intravenous drug use, diagnosis, and date of onset of symptoms for patients. In the heterosexual interview study, all living heterosexual patients with the syndrome whose cases had been reported as of 1 June 1982 were interviewed and asked to provide serum, urine, and saliva samples. The interviewers were the same physicians used in the national case-control study (1), and the same questions were asked. Additional questions were asked about exposure to known risks or risk groups. Interview data from homosexual male patients in the case-control study (1) were used for comparison. Laboratory data were obtained from specimens taken from homosexual and heterosexual patients and tested in laboratories at the CDC. Laboratory testing methods were previously reported (9).

Statistical testing was done with the chi-squared analysis only between groups within a data set. Patients who had more than one risk factor were placed only in one risk group for data analysis; these patients were placed in the first appropriate group, in the order homosexual, intravenous drug user, Haitian, and no identified risk.

Results

SURVEILLANCE DATA

Of the 377 patients with the acquired immunodeficiency syndrome whose cases were reported as of 1 June 1982, 80% were homosexual or bisexual men, 17% were heterosexual men and women, and 3% were men of unknown sexual orientation. Sixty-one percent of the 64 heterosexual patients were intravenous drug users, 25% were Haitian, and 14% had no identified risk. Differences in race and diagnoses were seen among the risk groups (Table 1). White patients composed a significantly greater proportion of the homosexual or bisexual group than any other risk groups ($p < 0.05$), and most intravenous drug users (72%) and patients with no identified risk (56%) were black (non-Haitian) or Hispanic. Kaposi's sarcoma af-

ected a significantly higher proportion of homosexual patients (34%) than intravenous drug users (3%) or Haitians (6%) ($p < 0.05$), whereas pneumocystis pneumonia was diagnosed significantly more frequently in intravenous drug users (77%) than in homosexuals (44%) ($p < 0.05$). Other opportunistic infections (most notably central-nervous-system toxoplasmosis) were found significantly more often in Haitians (44%) than in other risk groups ($p < 0.05$). Patients with both Kaposi's sarcoma and pneumocystis pneumonia were almost exclusively homosexual or bisexual men (98%).

INTERVIEW DATA

Of the 64 heterosexual patients who had the syndrome, we interviewed 31. Of those not interviewed, 27 had died before initiation of our study, 3 were too ill to interview, 1 refused, and 2 were lost to follow-up. Of the 31 patients interviewed, 24 were men and 7 were women; 22 were intravenous drug users, 4 were Haitian, and 5 had no identified risk.

A comparison of the socioeconomic status and history of drug use, sexual practices, and sexually transmitted diseases by risk group is presented in Table 2. The mean number of years of school was greater for homosexual patients. Heterosexual patients were more likely to have been married and less likely to earn \$20 000 or more annually or to have had a sexually transmitted disease compared with homosexuals. Intravenous drug users were the only patients to use heroin and cocaine intravenously; homosexual men were more likely to have used nasal cocaine than were heterosexual patients. A history of marijuana use was common in all risk groups, but a history of ever having used inhaled nitrites and ethyl chloride was common only in homosexual men.

Heterosexual patients from all risk groups reported considerably fewer sexual partners than did homosexual men, both for the year before onset of illness and for lifetime. In addition, sexual practices found to be frequent among homosexual men were rare among heterosexual risk groups. Few heterosexual patients were ex-

Table 2. Interviewed Patients with the Acquired Immunodeficiency Syndrome Compared by Risk Group, Socioeconomic Status, and History of Drug Use, Sexually Transmitted Diseases, and Sexual Practices

	Heterosexual Patients			Total (n = 31)	Homosexual or Bisexual Men (n = 50)*
	Intravenous Drug Users (n = 22)	Haitians (Men Only) (n = 4)	No Identified Risk (n = 5)		
Socioeconomic status					
Mean education, yrs	11.2	13.5	10.8	11.4	15.0
Annual income > \$20 000, n(%)	0	0	0	0	18(36)
Ever married, n(%)	10(45)	4(100)	3(60)	17(55)	9(18)
Drug use, n(%)†					
Heroin (intravenous)	22(100)	0	0	22(71)	0
Cocaine (intravenous)	21(96)	0	0	21(65)	0
Cocaine (nasal)	0	1(25)	2(40)	3(10)	33(66)
Marijuana (smoked)	15(68)	1(25)	5(100)	21(68)	44(88)
Nitrites (inhaled)	4(18)	0	0	4(13)	48(96)
Ethyl chloride (inhaled)	1(5)	0	0	1(3)	25(50)
Sexually transmitted disease, n(%)					
Gonorrhea	8(36)	1(25)	3(60)	12(39)	43(86)
Syphilis	2(9)	0	0	2(6)	34(68)
Mononucleosis	0	0	0	0	7(14)
Hepatitis (all types)	3(14)	0	0	3(10)	31(62)
Sexual practices (men/women)					
Exposure to feces during sex, n(%)‡					
Inserted penis into partner's rectum	3(17)/...	1(25)/...	0/0	4(13)	49(98)/...
Inserted tongue into partner's rectum	0/0	0/...	0/0	0	39(78)/...
Inserted hand into partner's rectum	0/0	0/...	0/0	0	26(52)/...
Exposure to semen or rectal trauma during sex, n(%)†					
Inserted partner's penis in mouth	0/1(25)	0/...	0/1(33)	2(6)	49(98)/...
Inserted partner's penis in rectum	0/1(25)	0/...	0/0	1(3)	47(94)/...
Inserted partner's hand in rectum	0/0	0/...	0/0	0	9(18)/...
Sexual partners, n					
Year before illness (median)	1/1	4/...	3/2	2	68
Lifetime (median)	40/8	81/...	23/8	41	1160

* Data from Jaffe and colleagues(1).

† Patients were asked if they ever used any of the drugs.

‡ Only exposure in the year before onset of illness was recorded.

posed to feces during sex or had rectal trauma. None of the heterosexual men was exposed to semen. Only 1 of the interviewed heterosexual patients had a history of parasitic diarrhea.

Haitians and Patients with No Identified Risk: We interviewed four Haitian patients and five patients with no identified risk. None had had a blood transfusion or a tattoo. Before onset of his illness, one Haitian had worked for an agency that collected blood, but he did not handle blood. These nine patients did not go to homosexual bars or bathhouses, nor did they socialize with homosexual men or persons who used intravenous drugs. No patient had had sexual contact with a person known to be an intravenous drug user. The female patients did not have sexual contact with men known to be bisexual. One patient with no identified risk had visited Haiti within 2 years of illness onset; he had worked with Haitian men and women and had had sexual contact with Haitian women, both in Haiti and the United States. This patient also had had sexual contact with a female prostitute in New York. The other male patient with no identified risk was a native Jamaican who had immigrated to the United States (New York) only 6 months before onset of his illness. The four Haitian patients had last resided in or visited Haiti 6 months, 2, 4, and 5 years, respectively, before illness onset. One woman with no identified risk

was a prostitute from New York, and one Haitian patient and one man with no identified risk (noted above) had had sexual contact with a female prostitute in New York 2 and 3 years, respectively, before illness onset.

Intravenous Drug Users: All except 1 of the 22 drug users interviewed admitted to sharing needles with other drug users. Only 2 men definitely knew that they had shared needles with homosexual men before their illness. None of the other heterosexual drug users had had close contact with men known to the homosexual or with Haitian men or women, or had visited Haiti. Seventeen patients were using drugs at the time of illness onset, but 5 patients stated that their last intravenous dose of drugs was more than 2 years before illness onset (range, 2 to 13 years).

LABORATORY RESULTS

We tested specimens from 100 homosexual patients (50 patients from the national case-control study [1] and 50 patients who were either dead or too ill to be interviewed, or who were interviewed after completion of the case-control study) and from 35 heterosexual patients (27 patients who were interviewed and 8 who died before being interviewed). We attempted to compare all patients with the acquired immunodeficiency syndrome by risk group and diagnosis for each set of laboratory data. Be-

Table 3. Herpes Virus Cultures and Serology in Heterosexual Patients with Pneumocystis Pneumonia by Risk Group, and in Homosexual Patients by Diagnosis

	Heterosexual Patients with Pneumocystis Pneumonia			Homosexual Patients			
	Drug User (n = 16)	Haitian (n = 9)	No Identified Risk (n = 8)	Pneumocystis Pneumonia (n = 26)	Kaposi's Sarcoma (n = 43)	Both Diseases (n = 14)	Other Infection (n = 6)
Geometric mean serum titers							
Cytomegalovirus/complement fixation antibody	15	22	30	38*	51	54	43
Cytomegalovirus/indirect hemagglutination antibody	1117	273	1290	2521†	2019	2957	724
Epstein-Barr virus/virus capsid antigen-IgG	190	159	154	143	350‡	313	172
Herpes simplex virus/complement fixation	13	23	17	16	24	21	17
Herpes simplex virus/indirect hemagglutination type 1	982	2806	5312	1314	2272	1663	470
Herpes simplex virus/indirect hemagglutination type 2	174	212	1579§	288	498	416	282
Patients cultured for cytomegalovirus, n tested/n positive (%)							
Site							
Urine	11/3(27)	4/3(75)	3/1(33)	20/9(45)	40/9(23)	13/3(23)	3/1(33)
Mouth	4/0	3/0	1/0	10/5(50)	28/3(11)	13/3(23)	3/1(33)
Mouth or urine	11/3(27)	4/3(75)	3/1(33)	22/13(59)	41/10(24)	15/5(33)	4/2(50)

* $p < 0.05$, compared with drug users.

† $p < 0.05$, compared with Haitians.

‡ $p < 0.05$, compared with homosexual men with pneumocystis pneumonia.

§ $p < 0.05$, compared with patients with pneumocystis pneumonia in other risk groups.

|| $p < 0.05$, compared with patients with Kaposi's sarcoma.

cause, in the heterosexual risk groups, we had sufficient data only for patients with the diagnosis of pneumocystis pneumonia, we compared only homosexual men by diagnosis and compared all patients with pneumocystis pneumonia by risk group.

Herpes Virus Results: We measured both complement fixation and indirect hemagglutination antibody titers to cytomegalovirus in 122 patients. Only 4 patients tested were negative for both: these 4 patients consisted of 3 drug users and 1 homosexual man, all with pneumocystis pneumonia. The mean titers were not significantly different among homosexual men with different diagnosis (Table 3). In patients with pneumocystis pneumonia, the mean complement fixation titer to cytomegalovirus was significantly higher for homosexual men than for drug users ($p < 0.05$), and the mean indirect hemagglutination antibody titer for homosexual men was significantly higher than that for Haitians ($p < 0.05$).

Only one patient, a homosexual man with pneumocystis pneumonia, had negative tests for IgG antibody to Epstein-Barr virus capsid antigen. Among homosexual patients, the mean titer was significantly higher for those with Kaposi's sarcoma than for those with pneumocystis pneumonia ($p < 0.05$). The mean titers for patients with pneumocystis pneumonia were not significantly different among the risk groups.

Five patients (two homosexual men and three drug users) had negative tests for herpes-simplex-virus complement fixation antibody. The mean titers were not significantly different among homosexual men with different diagnoses or among patients with pneumocystis pneumo-

nia in different risk groups. Mean titers for type-1 and type-2 herpes simplex virus-indirect hemagglutination antibody showed the same pattern, except for heterosexual patients with no identified risk, who had a significantly higher mean type-2 titer than did other risk groups ($p < 0.05$). Recovery rates for cytomegalovirus (Table 3) from urine alone were not significantly different among homosexual men with different diagnoses, but the virus was recovered more frequently from either the mouth or urine of homosexual patients with pneumocystis pneumonia than from those with Kaposi's sarcoma ($p < 0.01$).

Syphilis and Hepatitis A and B Serology: For syphilis testing, positive reactions to the rapid-plasma reagin were not significantly different among homosexual patients with different diagnosis or among patients with pneumocystis pneumonia in different risk groups (Table 4). However, a significantly greater proportion of homosexual (52%) than heterosexual (8%) patients ($p < 0.001$) had positive results on the microhemagglutination test for *Treponema pallidum*. No significant differences were found in the results from either serologic test for syphilis among homosexual patients in the four diagnostic categories.

There were no significant differences in positivity rates for either hepatitis A or B among risk groups or among homosexual patients with different diagnoses (Table 4). Antibody to hepatitis A was found in 80% of homosexual and 84% of heterosexual patients, whereas evidence of hepatitis B (antibody to surface or core antigen, or presence of surface antigen) was found in 96% and 84% of

Table 4. Syphilis and Hepatitis A and B Serology in Heterosexual Patients with Pneumocystis Pneumonia by Risk Group, and in Homosexual Patients by Diagnosis

	Heterosexual Patients with Pneumocystis Pneumonia				Homosexual Patients				Total
	Intravenous Drug User	Haitian	No Identified Risk	Total	Pneumocystis Pneumonia	Kaposi's Sarcoma	Both Diseases	Other Infection	
	← n tested/n positive (%) →								
Syphilis									
Rapid plasma reagin	12/0	5/3 (60)	7/2(29)	24/5(21)	22/4 (18)	41/13(32)	15/4 (27)	6/0	84/21(25)
Microhemagglutination	12/0	5/2 (40)	8/0	25/2 (8)	23/11(48)	45/27(60)	15/7 (47)	6/1(17)	89/46(52)*
Hepatitis A and B									
Hepatitis A antibody	18/16(89)	7/7(100)	6/3(50)	31/26(84)	25/21(84)	44/34(77)	14/13 (93)	6/3(50)	89/71(80)
Hepatitis B marker†	18/18(100)	8/6 (75)	6/3(50)	32/27(84)	25/25(100)	46/43(93)	12/12(100)	6/5(83)	89/85(96)

* $p < 0.05$, compared with total heterosexual patients.

† Hepatitis B surface antigen or antibody to hepatitis B surface or core antigen.

these two groups, respectively.

Serum Immunoglobulin Levels: The geometric mean serum levels of IgA were consistently above normal for patients with pneumocystis pneumonia in all risk groups (Table 5); 50% or more of patients with pneumocystis pneumonia in each risk group had elevated serum IgA levels. Levels of IgA were also significantly higher in homosexual patients with pneumocystis pneumonia than in those with Kaposi's sarcoma ($p < 0.05$). However, serum IgG levels showed a different trend; the geometric mean titer in homosexual men with Kaposi's sarcoma was significantly greater than that in homosexual men with pneumocystis pneumonia or other infections ($p < 0.05$). The geometric mean IgG titers for homosexual men, intravenous drug users, and patients with no identified risk with pneumocystis pneumonia were within normal limits. Haitian patients had a significantly higher geometric mean titer of IgG than did homosexual patients with pneumocystis pneumonia ($p < 0.05$).

Discussion

Our surveillance and interview data show a different profile for heterosexual and homosexual patients with the acquired immunodeficiency syndrome. Homosexual patients are more likely to be white, have a diagnosis of Kaposi's sarcoma, have more years of education, and earn higher salaries than are heterosexual patients. Heterosexual patients are more likely to be black, Hispanic, or Haitian. Non-Haitian heterosexual patients are more likely than homosexual patients to have a diagnosis of

pneumocystis pneumonia and to use intravenous drugs. The racial differences noted between homosexual patients and drug users may simply reflect the relative proportions in these risk groups, but denominator data are lacking.

The risk factors found by Jaffe and colleagues (1) for homosexual patients with the acquired immunodeficiency syndrome (a history of syphilis, hepatitis, or parasitic diarrhea; frequent use of inhaled nitrites; many sexual partners; and exposure to semen, feces, and rectal trauma during sexual intercourse) were reported rarely by heterosexual patients in our study. Although we cannot validate the responses of the interviewed patients, the consistent differences between homosexuals and patients in other risk groups suggest that risk factors for the acquired immunodeficiency syndrome differ between homosexual and heterosexual patients.

The interview data showed little reported interaction between risk groups. Because some heterosexual and homosexual intravenous drug users share needles, the needles may be a possible means of transmission of an infectious agent between these two groups. However, the reasons that Haitians and patients in no identified risk group are at risk for the syndrome remain unclear. These patients' sexual patterns and histories of drug use were different from those of other risk groups, and these patients' reported exposure to blood or blood products was rare. However, because we only interviewed four Haitian patients and five patients with no identified risk, our data are insufficient to draw conclusions. We also do not know

Table 5. Serum IgA and IgG Levels* in Heterosexual Patients with Pneumocystis Pneumonia by Risk Group, and in Homosexual Patients by Diagnosis

	Heterosexual Patients with Pneumocystis Pneumonia			Homosexual Patients			
	Intravenous Drug User (n = 18)	Haitian (n = 9)	No Identified Risk (n = 8)	Pneumocystis Pneumonia (n = 28)	Kaposi's Sarcoma (n = 49)	Both Diseases (n = 16)	Other Infection (n = 7)
IgA							
Geometric mean titer, mg/dL	574	444	342	494	293†	280	399
Patients above normal, n (%)	12(67)	5(56)	4(50)	18(64)	18(37)	5(31)	3(43)
IgG							
Geometric mean titer, mg/dL	1393	1984†	1390	1312	1859†	1366	1183
Patients above normal, n (%)	3(17)	7(78)	3(38)	8(29)	26(53)	7(44)	1(14)

* Normal levels = 85 to 385 mg/dL for IgA and 564 to 1765 mg/dL for IgG.

† $p < 0.05$, compared with homosexual patients with pneumocystis pneumonia.

if these patients are representative of their risk groups. We were limited to interviewing patients who were living and able to speak at the time of our study.

Our laboratory results included data from 50 homosexual patients whose cases were previously reported (9) and from an additional 50 homosexual and 35 heterosexual patients who fit our definition for acquired immunodeficiency syndrome. In total, we tested specimens from 100 of 300 homosexuals, 18 of 39 drug users, 9 of 16 Haitians, and 8 of 9 patients with no identified risk reported at the time of this study. All the reported serologic tests were done on 69% of the specimens from heterosexual patients and 84% of the specimens from homosexuals. Insufficient sera for complete testing presumably occurred in a random manner.

Interestingly, differences exist between patients with different diagnoses. Antibody titers to Epstein-Barr virus and serum immunoglobulin levels were significantly higher in patients with Kaposi's sarcoma than in those with pneumocystis pneumonia; conversely, serum IgA levels and the rate of recovery of cytomegalovirus were significantly greater in patients with pneumocystis pneumonia. The reasons for these differences are unknown but may include different degrees of immunosuppression in patients with different diagnoses or a different response to either the ongoing disease process or the theoretical causal agent of the immunosuppression.

Significant differences were also noted among patients with the same diagnosis in different risk groups. Positivity rates for serologic tests for syphilis and antibody titers to cytomegalovirus were higher in homosexual patients with pneumocystis pneumonia than in patients with this diagnosis in other risk groups, possibly reflecting life-style-related exposures.

The differences noted in diagnoses among the risk groups suggest at least two hypotheses. First, the manifestation of disease among risk groups may depend on the groups' previous exposures to infectious or toxic agents, or both. With suppression of the cell-mediated immune system, any latent microorganisms may reactivate. For example, in Haitian patients, the "other" infection (aside from Kaposi's sarcoma and pneumocystis pneumonia) is

usually central-nervous-system toxoplasmosis (probably reactivated), a disease that is commoner in Haiti than it is in the United States (CDC. Unpublished data). The second hypothesis is that the mode of acquisition of the causal agent of immunosuppression may affect the manifestation of disease, assuming that the disease is transmitted sexually to homosexual men, through blood to drug users, and by an unknown mechanism to Haitians. It is intriguing that Kaposi's sarcoma is much more likely to occur in homosexual patients; further investigation of exposures in this group may contribute to the understanding of the etiologic process of this tumor.

We conclude that risk factors for the acquisition of the acquired immunodeficiency syndrome are different for homosexual and heterosexual patients. Studies of these patients should include analyses by risk group and diagnosis.

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